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10/650,591	08/27/2003	Noubar B. Afeyan	COTH-P02-001	7918

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ROPES & GRAY LLP
IPRM - Floor 43
Prudential Tower
800 Boylston Street
Boston, MA 02199-3600

EXAMINER

MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
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1652

NOTIFICATION DATE	DELIVERY MODE
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ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No. 10/650,591	Applicant(s) AFEYAN ET AL.	
	Examiner MD. YOUNUS MEAH	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-5,19-34,37-40,42 and 43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,19, 21-34,37-40,42 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 3-5, 19-34, 37-40, 42 and 43 are pending. With supplemental amendment of this application, the applicant, on 03/05/010 amended claim 1, cancel claims 20 and added new claims 42-43.

Continued Examination under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' response of 4/2/10 is acknowledged. Applicants' arguments filed on 03/05/10 have been fully considered but they are found unpersuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Since a zymogen could be an inactive protease, claim 3 will be included in the elected group and will be examined. Since claims 28-29 comprise elected subject matter, claims 28-29 will be examined with the elected group. Claims 1, 3-5, 19, 21-34, 37-40, 42 and 43 are for examination.

Objection

Claims 1 and 42 are objected for reciting "posttranslational". It should be "post translational". Appropriate correction is required.

Claim Rejection 35 U.S.C 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, 19, 21-34, 37-40, 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, 19, 21--34, 37-40, 42 and 43 are indefinite in the recitation of the phrase "one amino acid substitution" for the following reason: It is unclear where the amino acid substitution is made within the adzyme. One needs to know the reference adzyme to compare to it for determining if a substitution is present. For examination purpose at least one amino acid substitution will be ignored. Correction is required.

Claim Rejections 35 U.S.C 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 19, 21-34, 37-40, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-5, 19, 21-34, 37-40, 43 (depend on claim 1) and 42 directed to any adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being a fusion

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complex comprising a protease, which catalyzes the proteolytic cleavage of a substrate polypeptide, conjugated to the constant portion of an immunoglobulin heavy chain and any targeting domain from any source having any structure conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises post translational modifications.. These claims are directed to a genus of fusion proteins of a protease conjugated with a genus of targeting domains having any structure from any source and antibodies comprising immunoglobulin heavy chains, wherein said targeting domain or antibody is post translationally modified in any way to inhibit auto-cleavage by said protease. The specification at paragraph 0440 states that protease vulnerable sites may be post-translationally modified by phosphorylation, methylation or glycosylation chemically in-vitro. In order to inhibit the protease cleavage of a protein by post translational modification wherein said modification is done chemically in-vitro by phosphorylation, methylation or glycosylation reaction in-vitro, one would require knowledge of the tertiary protein structure and the availability of the cleavage site so that such modification could be targeted selectively to the protease cleavage site without affecting other site(s)/amino acids of the protein. Neither the specification nor the prior art teaches post-translational modification of a protease cleavage site of any protein by a chemical reaction without affecting other sites/amino acids of the protein. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 3-5, 19, 21-34, 37-40, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an adzyme or bifunctional fusion protein wherein prethrombin is conjugated via a linker with scFv α HA (antibody) or mesotrypsin is conjugated via a linker with sp55 of TNFR1, \square does not reasonably provide enablement for any adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being a fusion complex comprising a protease, which catalyzes the proteolytic cleavage of substrate polypeptide, conjugated to a constant portion of an immunoglobulin heavy chain and any targeting domain conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises any post translational modification to inhibit autoproteolysis by said protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-5, 19, 21-34, 37-40, 43 (depend on claim 1) and 42 are so broad as to encompass any adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being a fusion complex comprising a protease, which catalyzes the proteolytic cleavage of a substrate polypeptide, conjugated to the constant portion of an immunoglobulin heavy chain and any targeting domain from any source having any

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structure conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises a post translational modification. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number adzymes or fusion proteins conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises post translational modifications to inhibit auto-cleavage by the said protease. These claims are drawn to adzymes having a post-translational modification anywhere within the structure of the [adzyme]. The specification at paragraph 0440 states that protease vulnerable sites may be post-translationally modified by phosphorylation, methylation or glycosylation chemically in vitro. For such a modification, detailed structure of the protein is required so that post-translational reaction can be targeted selectively to the protease cleavage site. Without sufficient information of the structure of the adzyme one of ordinary skilled in the art requires undue experimentation to ascertain protease cleavage site so that it can be chemically modified without modifying other part of the protein. Moreover if the protease cleavage site is identified in a known structure of an adzyme, one of ordinary skilled in the art requires undue experimentation to exactly modify said cleavage site without affecting other parts of the protein. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins'

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structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only few fusion proteins of specific amino acid sequences.

The specification does not support the broad scope of the claims which encompass any fusion protein made via conjugation of a protease with a broad class of targeting domains conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises post translational modifications by any method to inhibit auto-cleavage by said protease, because the specification does **not** establish:

(A) regions of the protein structure which may be modified by post translational modification without effecting adzyme activity; (B) the general tolerance of targeting domain activity to post translational modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues of the adzyme with an expectation of obtaining the desired protection against proteolysis; and (D) sufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly include any fusion proteins that made via conjugation of a protease with a broad class of targeting domains conjugated to the constant portion of an immunoglobulin heavy chain wherein said adzyme comprises post translational modifications obtained by any method to inhibit auto-cleavage by said protease domain. The scope of the claims must bear a reasonable correlation with the

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scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of adzyme activity, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection of Claims 1, 3-4, 21-27, 30-34 and 37 under 35 U.S.C. 103(a) by Davis et al (WO00/64485) in view of Chamow et al (Trend Biotech, 1996, 14, pp52-60) as discussed in the prior office action is withdrawn after amendment of claim 1. However Davis et al (WO00/64485) and Chamow et al (Trend Biotech, 1996, 14, pp52-60) are used in a new rejection as described below:

Claims 1, 3-5, 21--34, 37 42-43 are rejected under 35 U.S.C. 103(a) by Davis et al (WO00/64485) in view of Chamow et al (Trend Biotech, 1996, 14, pp52-60) and Sallberg et al (U.S. Patent No. 6960569).

As explained in the 35 USC 112 2nd paragraph rejection, in claim 1 no patentable weight to the term "amino acid substitution" has been given. Even if the limitation were to be given patentable weight, substitutions in the cleavage site are obvious because,

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Davis et al, as shown below teach amino acid substitution in a fusion protein and it is well known in the art to mutate protease cleavage site to make a protein resistant to protease cleavage (see Sallberg et al) and it is obvious for one of ordinary skill in the art to substitute amino acid residues at a protease cleavage site to protect the adzyme from autodegradation. Davis et al. teach fusion proteins wherein enzymes (serine protease, (teach applicants' claim 4), chymotrypsin, matrix metalloprotease, etc) which catalyze degradation of a target are conjugated to targeting (bind to the target) domains, such as a ligand or antibody (page 23, lines 15-30, page 8 lines 20-25, page 15 lines 9-52, wherein protease is conjugated to immunoglobulin, Fab or F(ab)₂) and wherein said protease comprises one or more amino acid substitutions (page 4). Davis et al teach that resulting chimeric protein has greater (catalytic, page 8) activity than the unconjugated molecule. The chimeric protein of Davis et al. binds to the target and antagonize/inhibit /degrade a wide variety of receptors and/or intermediary signaling molecules such as cytokines, EGF-like factors, etc (page 28) and degrade component of soil (page 5, inherently comprises insoluble protein complex) . Davis et al. use the fusion protein as a pharmaceutical composition (pages 51-56).

However Davis et al do not teach a fusion complex comprising a protease conjugated to constant portion of immunoglobulin heavy chain and second fusion protein comprising a targeting domain conjugated to constant portion of an immunoglobulin heavy chain. Although Davis et al teach amino acid substitutions in a fusion protein, Davis et al does not teach said substitution to inhibit auto-cleavage by said protease domain.

Sallberg et al. (US 6960569) teach mutated NS3/4A comprising NS3 protease (a serine protease) conjugated to HCV antibody (SEQ ID NOs 3-11, column 3) wherein proteolytic cleavage site is mutated and said mutant NS3/4A fusion protein is highly immunogenic (column 5).

Chamow et al teach bispecific immunoadhesins (immunoglobulin fusion protein) comprising two different proteins having different functions each conjugated to each pair of constant regions of immunoglobulins (table 1 and Fig 3, P-selectin-IgG and E-selectin-IgG). It is well known in the art the advantages of using the immunoglobulin constant region to make fusion proteins (see, Chamow et al, Trend Biotech, 1996, 14, pp52-60, and Ashkenazi et al, Current Opin. of Immunol. 1997, 9, pp 195-200): such as that joining the fusion partner to immunoglobulin facilitates proper folding of domains and function (page 52 right column 2nd parag. Chamow et al) by providing antibody type structural properties (by bring them closer, Ashkenazi et al, page 196 left column 2nd parag) and increased size often extend in vivo half-life (Ashkenazi et al, page 196 left column 2nd parag.). Therefore, one of skill in the art would have been **motivated** to make the fusion complex comprising a stable protease conjugated to constant portion of immunoglobulin heavy chain and a targeting domain conjugated to constant portion of an immunoglobulin heavy chain so that said catalytic domain and targeting domain fusion complex comprise proper folding (via immunoglobulin dimeric binding partner) and the fusion protein would lack a proteolytic cleavage site (as described by Sallberg

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et al.) to inhibit auto-cleavage by said protease and so that their effective concentration and function is optimized at the target site.

As such it would have been obvious to one of ordinary skill in the art to use a protease to make a fusion protein (adzyme) as taught by Davis et al and Chamow et al, wherein the protease is conjugated to the constant region of an immunoglobulin heavy chain and a targeting domain comprising an antibody light chain is conjugated to the constant portion of another immunoglobulin heavy chain and said adzyme lacks a proteolytic cleavage site (as taught by Sallberg et al.) to inhibit auto-cleavage by the protease and use the resulting adzyme to inactivate substrate polypeptides by catalyzing the proteolytic cleavage of the said substrate polypeptide. One of ordinary skill in the art at the time of the invention was made would have had a reasonable expectation for success for making an adzyme comprising a fusion complex comprising the protease conjugated to constant portion of immunoglobulin heavy chain and a targeting domain conjugated to constant portion of an immunoglobulin heavy chain, because the DNA encoding a protease is known, and the molecular biology techniques required to make a recombinant fusion proteins are well known in the art (Ashkenazi et al, Current Opin. of Immunol. 1997, 9, pp 195-20). Claims 4, 21-22, and 30-34 are included in rejection because of the reason explained below: Claim 4 requires the protease domain to be a specific protease such as a metalloprotease, which is taught by Davis et al. With regard to claims 21-22, Davis et al teach that the substrate can be receptors, signaling molecules like cytokines, EGF-like factors, etc., which are compounds found in a biological fluid of an animal, including blood. Those compounds

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are endogenous to a human patient (claim 30). With regard to claims 31-32, Davis teaches cytokines as substrates that can be targeted by the adzyme, and since the specification teaches that a substrate that is not significantly affected by the presence of serum albumin is a cytokine, as evidenced by claim 23 of the instant application, Davis teaches that limitation. With regard to claims 33-34, since the adzyme of Davis and Chamow would degrade cytokines, it follows that the half life of the cytokine would be reduced as it would be degraded. Furthermore, by degrading the cytokine, it would necessarily disrupt the interaction between the cytokine and a receptor.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (WO 00/64485) in view of Chamow et al (Trend Biotech, 1996, 14, pp52-60) and Sallberg et al. (US 6960569) as applied to claims 1, 4, 19-27, 30-34 and 37 above, and further in view of Dolinar et al. (*Food tecnol and biotech.* 2000, 38, 5-9).

Davis et al., Sallberg et al. and Chamow et al are described above. However neither Davis et al. nor Chamow et al. teach purification of a fusion protein comprising a protease domain using a reversible protease inhibitor.

Use of protease inhibitor in protein purification is well known in prior art. Dolinar et al. teach MMTS (methyl methane-thiosulfonate), a reversible protease inhibitor in the purification and refolding of a cystine proteinase type protein (page 6, column 2 last parg.). Therefore, one of skill in the art would have been **motivated to** purify a fusion protein complex comprising a protease using a protease inhibitor so that said fusion protein complex would not be cleaved by the protease.

As such it would have been obvious to one of ordinary skill in the art to use a protease inhibitor to purify the protease-containing fusion protein complex of Davis et al. and Chamow et al. described above. One of ordinary skill in the art has a reasonable expectation of success at is obtaining an adzyme which is resistant to autocatalytic proteolysis in view of the teachings of Dolinar et al. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Claims 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (WO 00/64485) in view of Chamow et al (Trend Biotech, 1996, 14, pp52-60) and Sallberg et al. (US 6960569) as applied to claims 1, 4, 19-27, 30-34 and 37 above, and further in view of Sanderson et al. (Medic. Res Rev 1999, 19, 179-197):

Davis et al., Sallberg et al. and Chamow et al. are described above. However, neither Davis et al. nor Chamow et al. nor Sallberg et al. teach a pharmaceutical preparation comprising a reversible inhibitor safe to humans.

Sanderson *et al.* (Medic. Res Rev 1999, 19, 179-197) teach a small molecule non-covalent binding protease inhibitor used in a pharmaceutical composition which is reversible and safe to humans (abstract).

Use of protease inhibitors in protein samples is well known in prior art because proteases catalyze the degradation of protein molecules (abstract, page 1, Sanderson et al.). Therefore, in order to inhibit the protease degradation of a pharmaceutical preparation comprising the adzyme of Davis et al. and Chamow et al., one of skill in the

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art would have been **motivated** to add a reversible protease inhibitor that is safe to humans as taught by Sanderson *et al.* to extend the shelf life of the adzyme.

As such it would have been obvious to one of ordinary skill in the art to make a pharmaceutical preparation comprising the adzyme of Davis *et al.* and Chamow *et al.* and combine it with a reversible protease inhibitor as taught by Sanderson *et al.* so that said pharmaceutical preparation is safe to humans and remains effective. One of ordinary skill in the art has a reasonable expectation of success at making such pharmaceutical composition in view of the fact that protease inhibitors which are safe for humans are known and used in the art as evidenced by Sanderson *et al.* Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made.

Argument

Applicants' arguments filed on 03/05/010 have been fully considered, but they found unpersuasive. Applicants argue that their invention is not disclosed nor suggested by the cited prior arts and that the skilled person would have little expectation of success in combining the cited references to derive their invention. Applicants argue that Davis *et al.* do not teach fusion proteins comprising constant portion of an immunoglobulin heavy chain and Chamow *et al.* do not teach fusion protein comprising protease domain. Applicants' arguments have been fully considered, but they found unpersuasive. If Davis *et al.* teach a fusion protein comprising a protease and the constant portion of an immunoglobulin heavy chain or Chamow *et al.* teach a fusion

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protein comprising a protease domain and an immunoglobulin heavy chain, these references would anticipate applicants' invention. As explain above, it is obvious to make a fusion protein (adzyme) as taught by Davis et al and Chamow et al, wherein a protease is conjugated to the constant region of an immunoglobulin heavy chain and a targeting domain comprising an antibody light chain is conjugated to the constant portion of another immunoglobulin heavy chain and use the resulting adzyme to inactivate substrate polypeptides by catalyzing the proteolytic cleavage of the said substrate polypeptide.

Applicants argument for the rejection of claim 5 regarding the use of Dolinar et al in combination of Davis et al. and Chamow et al. is fully considered, but it is found unpersuasive. Dolinar et al teach protease inhibitor in the purification process of proteins, therefore it would have been obvious to use protease inhibitor to purify fusion protein of Davis et al. or Chamow et al. as described above.

Applicants argument for the rejection of claims 38-40 regarding the use of Sanderson *et al.* in combination of Davis et al., and Chamow et al. is fully considered, but it is found unpersuasive. Sanderson *et al.* teach a small molecule non-covalent binding protease inhibitor used in a pharmaceutical composition which is reversible and safe to humans (abstract). Use of protease inhibitors in protein samples is well known in prior art because proteases catalyze the degradation of protein molecules (abstract, page 1, Sanderson et al.). Therefore, in order to inhibit the protease degradation of a pharmaceutical preparation comprising the adzyme of Davis et al. and Chamow et al., one of skill in the art would have been **motivated** to add a reversible protease inhibitor

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that is safe to humans as taught by Sanderson *et al.* to extend the shelf life of the adzyme. Regarding applicants' argument against the rejection of 4, 21-22 and 30-34, applicants' argument has been considered and the reasons why the limitations recited in these claims are obvious over the cited references are explained in the 103(a) rejection above.

Double Patenting Rejection

The provisional rejection of claims 1, 3-5, 19, 21-29, 30-34, 37-40, 42-43 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-5, 19-27, 30-34, 37-40 of copending Application No.10/792498 is maintained.

Examiner agrees with applicant that the provisional double patenting rejections may be withdrawn when all claims are otherwise allowable if the copending application is not allowable. All the examined claims of the instant application are rejectable on other grounds. Since applicant did not submit terminal disclaimer, the rejections are be maintained.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Examiner, Art Unit 1652

/Delia M. Ramirez/
Primary Examiner, Art Unit 1652